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Detection of the PEBP2β/MYH11 Fusion Transcript in Acute Myelomonoblastic Leukemia (M4Eo) Supervening in a Patient With Adult T-Cell Leukemia

To the Editor: We present a case of acute myelomonoblastic leukemia with marrow eosinophilia (M4Eo) having inv(16) developed after etoposide administration for chronic type adult T-cell leukemia (ATL). A 74-year-old Japanese woman was admitted in April 1993 because of a fungal infection on the chest skin that occurred 5 months before. The leukocyte count was 28.9×10^9/l with 61% abnormal lymphocytes showing lobulated nuclei and expressing CD4 antigen. The serum was positive for anti-HTLV-I antibody. She was diagnosed as chronic type ATL and treated with two courses of 75 mg of etoposide orally for 21 days. The leukocyte counts decreased

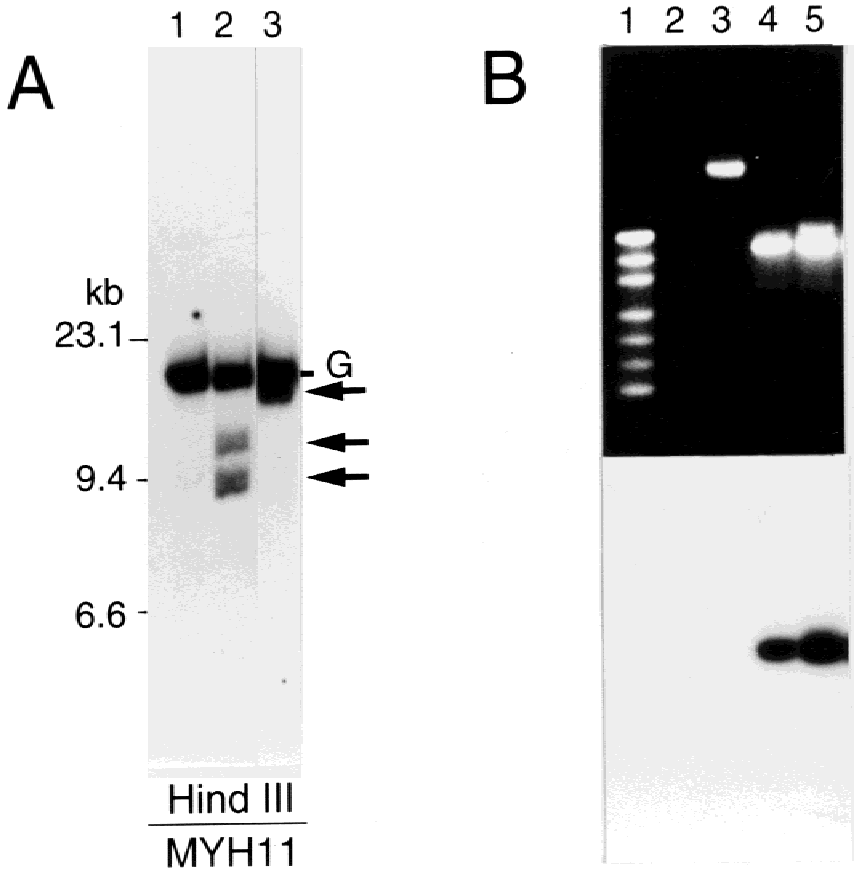

Fig. 1. A: Southern blotting to detect MYH11 gene rearrangement. Arrows show rearranged bands. G: germline. Lanes 1: K562 as a negative control, 2: ME-1 having inv(16) as a positive control; 3: patient. B: RT-PCR analysis of PEBP2β/MYH11 fusion transcripts. Top shows ethidium bromide staining. Bottom shows Southern blotting hybridized with internal oligonucleotides to verify specificity of the amplified bands. Lanes 1: size marker (pUC19/HpaII), 2: water, 3: K562 cell line; 4: ME-1 cell line; 5: patient.

to less than 10×10^9/l for 14 months. In October 1994, a hemoglobin level and platelet counts decreased to 7.5 g/dl and 43×10^9/l, respectively. The leukocyte count was 8.0×10^9/l with 27% blasts, 28% monocytes, 25% lymphocytes, and 10% abnormal lymphocytes. The bone marrow was hypercellular with 58.6% blasts and 24.2% eosinophils having abnormal basophilic granules. The blasts had Auer bodies and were positive for myeloperoxidase, butyrate esterase, and chloroacetate esterase stainings. She was diagnosed as M4Eo. Serum and urine lysozyme levels were elevated to 49.8 and 19.1 mg/l, respectively. The blasts were positive for CD2, CD13, CD33, CD34, CD38, CD117, and HLA-DR antigens. All 20 metaphases examined revealed 46,XX,inv(16)(p13q22),+22. We detected MYH11 gene rearrangement by Southern blotting (Fig. 1A) and PEBP2β/MYH11 fusion transcripts by reverse transcriptase-polymerase chain reaction (RT-PCR) analysis (Fig. 1B). Monoclonal integration of HTLV-1 was also found by Southern blotting. She received no chemotherapy because of her poor general condition and died of pneumonia in December 1994.

Some possible explanations for the M4Eo supervening ATL in this patient include (1) coincidental complication, (2) the high frequency of other malignancies in the ATL patients [1], and (3) therapy-related leukemia (TRL). It is possible that the M4Eo in this case was induced by the etoposide used in chemotherapy for ATL. Although the cumulative etoposide dose in this case was only 3,100 mg/m^2, continuous administration carries a high risk of TRL [2]. The immune system to malignancy altered by HTLV-I infection may increase a risk of TRL. Unfortunately, we could not examine any cytogenetic or molecular study at the time of initial diagnosis of ATL. Common chromosome aberrations in epipodophillotoxin-related AML involve 11q23 or 21q22. Inv(16) has been reported in 16 cases of TRL [3]. Almost all chromosome aberrations found in de novo AML are now also found in TRL. The affected genes among the chromosome aberrations in TRL are thought to be the same as in de novo AML. However, inv(16)(p13q22) has also been detected in adenocarcinoma cells of sigmoid colon [4]. The 16q22 region around the breakpoint of inv(16) has been reported as a fragile site [5]. In this case, we demonstrated that the PEBP2β and MYH11 genes are involved in inv(16) of TRL as well as de novo AML.

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References

1. Asou N, Kumagai T, Uekihara S, Ishii M, Sato M, Sakai K, Nishimura H, Yamaguchi K, Takatsuki K: HTLV-I seroprevalence in patients with malignancy. Cancer 58:903–907, 1986.
2. Pui CH, Ribeiro RC, Hancock ML, Rivera GK, Evans WE, Raimondi SC, Head DR, Behm FG, Mahmoud MH, Sandlund JT, Crist WM: Acute myeloid leukemia in children treated with epipodophillotoxins for acute lymphoblastic leukemia. New Engl J Med 325:1682–1687, 1991.
3. Quesnel B, Kantarrijian H, Bjergaard JP, Brault P, Estey E, Lai JL, Tilly H, Stoppa AM, Archimbaud E, Harousseau JL, Bauters F, Fenaux P: Therapy-related acute myeloid leukemia with t(8;21), inv(16), and t(8;16): A report on 25 cases and review of the literature. J Clin Oncol 11:2370–2379, 1993.
4. Shabtai F, Sternberg A, Klar D, Reiss R, Halbrecht I: Inversion (16)(p13q22) in tumor cells of sigmoid colon. Cancer Genet Cytogenet 27:171–175, 1987.
5. Murata M, Takahashi E, Ishihara T, Minamihisamatsu M, Takagi T, Kanako Y, Hori T: Heritable fragile sites and cancer: fra(16)(q22) in lymphocytes of an acute nonlymphocytic leukemia patient with inv(16)(p13q22). Cancer Genet Cytogenet 25:81–85, 1987.